



US006074647A

# United States Patent [19]

[11] Patent Number: **6,074,647**

Zimmerman et al.

[45] Date of Patent: **\*Jun. 13, 2000**

[54] **METHOD OF INCREASING SKIN CELL RENEWAL RATE USING ACEROLA CHERRY FERMENTATE**

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[\*] Notice: This patent is subject to a terminal disclaimer.

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[21] Appl. No.: **09/060,435**

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[22] Filed: **Apr. 14, 1998**

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[51] Int. Cl.<sup>7</sup> ..... **A61K 7/00**

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### [57] ABSTRACT

The present invention relates to a composition for topical use comprising an organic acid and acerola cherry fermentate. The present invention also relates to a method of enhancing the rate of skin desquamation by incorporating acerola cherry fermentate into a composition containing an organic acid. The composition can be topically applied.

**13 Claims, No Drawings**

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## METHOD OF INCREASING SKIN CELL RENEWAL RATE USING ACEROLA CHERRY FERMENTATE

### BACKGROUND OF THE INVENTION

The present invention relates to a composition to enhance the rate of skin cell renewal or exfoliation and to a method of increasing the skin cell renewal rate. In particular, the present invention relates to a composition containing one or more selected organic acids and an enhancing effective amount of acerola cherry fermentate. The present invention also relates to a method of increasing the rate of skin-cell renewal by applying a composition to the skin, wherein the composition comprises at least one selected organic acid, an enhancing effective amount of acerola cherry fermentate, and optionally, a suitable cosmetic vehicle.

With the aging population there is a continuing effort to provide cosmetic compositions to improve the appearance of the skin. Recently, many compositions have included hydroxycarboxylic acids such as glycolic, lactic, citric, and malic acids and are being marketed for such uses as dry skin, the reduction of wrinkles and fine lines and to combat the effects of aging. In addition, there is always a need for a composition to treat dry skin.

Human skin may be classified into two major parts: the outer layer or epidermis and an underlying layer or dermis. The dermis contains, among other things, blood vessels, nerves, collagen, elastin, and fibroblast cells, which are responsible for the biosynthesis of collagen and elastin.

The epidermis itself also may be considered to consist of two major zones, an inner or malpighian layer and an outer or horny layer. The malpighian layer, a living tissue, may be further divided into basal, spinous, and granular layers. The horny layer, a dead tissue, is also referred to as stratum corneum, which is the skin tissue one feels.

In the natural process, basal cells in the basal layer move outward through the spinous and granular layers to become dead cells called corneocytes, in the stratum corneum. The stratum corneum consists of approximately 14 layers of corneocytes. In the normal skin it takes about 14 days for the basal cells to move from the basal layer to the end of the granular layer and to become corneocytes, and another 14 days to reach the outermost layer of the stratum corneum, where they are naturally shed or exfoliated. This process of forming corneocytes is called keratinization, and stratum corneum are the natural products produced by this process. Usually, it takes about 28 days for cells of the basal layer to move outward to the surface in the course of making new skin.

It is thought that by increasing the natural exfoliation rate of the outermost part of the stratum corneum and thus exposing lower layers of the stratum corneum, the appearance of the skin will be improved. Many substances are known to increase the rate of natural exfoliation but recently hydroxycarboxylic acids have received an increasing amount of attention. A drawback to the use of hydroxycarboxylic acids is that they can irritate the skin of the user. Thus, it would also be desirable to increase the rate of exfoliation beyond that provided by the hydroxycarboxylic acid without further increasing the possibility of skin irritation.

### SUMMARY OF THE INVENTION

In accordance with the present invention, there is provided a composition for topical use comprising at least one

organic acid and acerola cherry fermentate. The acerola cherry fermentate is present in an amount effective to enhance the skin cell exfoliation rate of the organic acid. It is believed that the acerola cherry fermentate synergistically enhances the rate of skin exfoliation when combined with an organic acid, wherein the organic acid is preferably chosen from hydroxy carboxylic acids, keto carboxylic acids and mixtures thereof.

In accordance with this aspect of the present invention, there is provided a composition comprising at least one organic acid and acerola cherry fermentate present in a therapeutically effective amount in topically acceptable vehicle for application to human skin to enhance the rate of skin exfoliation provided by the organic acid.

Preferably, the composition can be used for the topical treatment and/or alleviation of dry skin and other skin maladies.

Although it is known that the acerola cherry fermentate contains a minor amount of organic acids and a minor amount of carboxylic acids, typically they are present in an amount no greater than about 5% by weight, preferably no greater than about 3%, and more preferably, no greater than about 2% of the acerola cherry fermentate. The acids include lactic, citric, malic, tartaric, ascorbic acids with lactic comprising about 92% by weight of all the acids. Surprisingly, it has been found that when the acerola cherry fermentate is combined with an organic acid, the exfoliation rate is increased beyond that which would be expected from the additional minor amount of acids found in the acerola cherry fermentate.

Surprisingly, the enhancement in the rate of skin exfoliation provided by the acerola cherry fermentate does not cause additional skin irritation.

The terms "minor amount of organic acids" and "minor amount of carboxylic acids" as used in the specification and accompanying claims means that any organic acid or carboxylic acid, which includes saturated and unsaturated carboxylic and dicarboxylic acids, hydroxymonocarboxylic acids, hydroxydicarboxylic acids, and hydroxytricarboxylic acids, is present in an amount no greater than about 5% by weight, preferably no greater than about 3%, and more preferably, no greater than about 2% of the acerola cherry fermentate.

In the composition according to the present invention, the amount of acerola cherry fermentate to be used can not be absolutely specified because it varies according to the form of preparation. However, it is generally used in an amount from about 0.01% to about 50%, more generally from about 0.1% to about 10%. Preferably the acerola cherry fermentate is used in an amount from about 0.5% to about 8%, more preferably from about 1% to about 5% based on the whole weight of the composition.

It is noted that, unless otherwise stated, all percentages given in this specification and the appended claims refer to percentages by weight.

### DETAILED DESCRIPTION OF THE INVENTION

In accordance with the present invention, a skin, hair, and nail composition is provided and comprises at least one organic acid and acerola cherry fermentate. In another aspect, the composition comprises one or more exfoliating agents, and acerola cherry fermentate to enhance the exfoliation effect of the exfoliating agents.

The organic acid is chosen from hydroxy carboxylic acids, keto carboxylic acids and mixtures thereof. The

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hydroxycarboxylic acids can be any of the known hydroxycarboxylic acids but are preferably 2-hydroxycarboxylic acids and related compounds. For convenience, the 2-hydroxycarboxylic acids and related compounds which may be used in accordance with this invention may be classified into three groups, namely (1) 2-hydroxycarboxylic acids, (2) 2-ketocarboxylic acids and esters thereof, and (3) other related compounds. The related compounds may include hydroxycarboxylic acids with the hydroxyl group at any position other than position 2, for example position 3, position 4 or position 5, as well as cyclic hydroxycarboxylic acids (e.g., ascorbic acid and quinic acid), and also may include ketocarboxylic acids and esters thereof. Preferred related compounds include 3-hydroxycarboxylic acids, and 2-ketocarboxylic acids and esters thereof.

## Group 1

The first group comprises organic carboxylic acids in which one hydroxy group is attached to the 2 position carbon atom of the acid. The generic structure of such 2-hydroxycarboxylic acids may be represented as follows:



where  $R_a$  and  $R_b$  may be the same or different and are independently selected from H, F, Cl, Br, alkyl, aralkyl or aryl group of saturated or unsaturated, isomeric or non-isomeric, straight or branched chain or cyclic form, having 1 to 29 carbon atoms, and in addition  $R_a$  and  $R_b$  may carry OH, CHO, COOH and alkoxy group having 1 to 9 carbon atoms. 2-Hydroxycarboxylic acids may be present as a free acid or lactone form, or in a salt form with an organic base or an inorganic alkali. 2-Hydroxycarboxylic acids may exist as stereoisomers as D, L, and DL forms when  $R_a$  and  $R_b$  are not identical.

Typical alkyl, aralkyl and aryl groups for  $R_a$  and  $R_b$  include methyl, ethyl, propyl, isopropyl, butyl, pentyl, octyl, decyl, dodecyl, hexadecyl, benzyl, and phenyl, etc. 2-Hydroxycarboxylic acids of the first group may be further divided into subgroups comprising (1) alkyl hydroxycarboxylic acids, (2) aralkyl and aryl hydroxycarboxylic acids, (3) polyhydroxy-carboxylic acids, and (4) hydroxypolycarboxylic acids. The following are representative 2-hydroxycarboxylic acids in each subgroup.

## (1) Alkyl Hydroxycarboxylic Acids

1. 2-Hydroxyethanoic acid (Glycolic acid, hydroxyacetic acid)  
(H) (H) C (OH) COOH
2. 2-Hydroxypropanoic acid (Lactic acid)  
(CH<sub>3</sub>) (H) C (OH) COOH
3. 2-Methyl 2-hydroxypropanoic acid (Methylactic acid)  
(CH<sub>3</sub>) (CH<sub>3</sub>) C (OH) COOH
4. 2-Hydroxybutanoic acid  
(C<sub>2</sub>H<sub>5</sub>) (H) C (OH) COOH
5. 2-Hydroxypentanoic acid  
(C<sub>3</sub>H<sub>7</sub>) (H) C (OH) COOH
6. 2-Hydroxyhexanoic acid  
(C<sub>4</sub>H<sub>9</sub>) (H) C (OH) COOH
7. 2-Hydroxyheptanoic acid  
(C<sub>5</sub>H<sub>11</sub>) (H) C (OH) COOH
8. 2-Hydroxyoctanoic acid  
(C<sub>6</sub>H<sub>13</sub>) (H) C (OH) COOH
9. 2-Hydroxynonanoic acid  
(C<sub>7</sub>H<sub>15</sub>) (H) C (OH) COOH

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10. 2-Hydroxydecanoic acid  
(C<sub>8</sub>H<sub>17</sub>) (H) C (OH) COOH
11. 2-Hydroxyundecanoic acid  
(C<sub>9</sub>H<sub>19</sub>) (H) C (OH) COOH
12. 2-Hydroxydodecanoic acid (Alpha hydroxylauric acid)  
(C<sub>10</sub>H<sub>21</sub>) (H) C (OH) COOH
13. 2-Hydroxytetradecanoic acid (Alpha hydroxymyristic acid)  
(C<sub>12</sub>H<sub>25</sub>) (H) C (OH) COOH
14. 2-Hydroxyhexadecanoic acid (Alpha hydroxypalmitic acid)  
(C<sub>14</sub>H<sub>29</sub>) (H) C (OH) COOH
15. 2-Hydroxyoctadecanoic acid (Alpha hydroxystearic acid)  
(C<sub>16</sub>H<sub>33</sub>) (H) C (OH) COOH
16. 2-Hydroxyeicosanoic acid (Alpha hydroxyarachidonic acid)  
(C<sub>18</sub>H<sub>37</sub>) (H) C (OH) COOH
17. 2-Hydroxytetraeicosanoic acid (Cerebronic acid)  
(C<sub>22</sub>H<sub>45</sub>) (H) C (OH) COOH
18. 2-Hydroxytetraeicosenoic acid (Alpha hydroxynervonic acid)  
(C<sub>22</sub>H<sub>43</sub>) (H) C (OH) COOH

## (2) Aralkyl and Aryl 2-Hydroxycarboxylic Acids

1. 2-Phenyl 2-hydroxyethanoic acid (Mandelic acid)  
(C<sub>6</sub>H<sub>5</sub>) (H) C (OH) COOH
2. 2,2-Diphenyl 2-hydroxyethanoic acid (Benzilic acid)  
(C<sub>6</sub>H<sub>5</sub>) (C<sub>6</sub>H<sub>5</sub>) C (OH) COOH
3. 3-Phenyl 2-hydroxypropanoic acid (Phenyllactic acid)  
(C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>) (H) C (OH) COOH
4. 2-Phenyl 2-methyl 2-hydroxyethanoic acid (Atrolactic acid)  
(C<sub>6</sub>H<sub>5</sub>) (CH<sub>3</sub>) C (OH) COOH
5. 2-(4'-Hydroxyphenyl) 2-hydroxyethanoic acid (4-Hydroxymandelic acid)  
(HO—C<sub>6</sub>H<sub>4</sub>) (H) C (OH) COOH
6. 2-(4'-Chlorophenyl) 2-hydroxyethanoic acid (4-Chloromandelic acid)  
(C1-C<sub>6</sub>H<sub>4</sub>) (H) C (OH) COOH
7. 2-(3'-Hydroxy-4'-methoxyphenyl) 2-hydroxyethanoic acid (3-Hydroxy-4-methoxymandelic acid)  
(HO—, CH<sub>3</sub>O—C<sub>6</sub>H<sub>3</sub>) (H) C (OH) COOH
8. 2-(4'-Hydroxy-3'-methoxyphenyl) 2-hydroxyethanoic acid (4-Hydroxy-3-methoxymandelic acid)  
(HO—, CH<sub>3</sub>O—C<sub>6</sub>H<sub>3</sub>) (H) C (OH) COOH
9. 3-(2'-Hydroxyphenyl) 2-hydroxypropanoic acid [3-(2'-Hydroxyphenyl) lactic acid]  
(HO—C<sub>6</sub>H<sub>4</sub>—CH<sub>2</sub>) (H) C (OH) COOH
10. 3-(4'-Hydroxyphenyl) 2-hydroxypropanoic acid [3-(4'-Hydroxyphenyl) lactic acid]  
(HO—C<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>) (H) C (OH) COOH
11. 2-(3',4'-Dihydroxyphenyl) 2-hydroxyethanoic acid (3,4-Dihydroxymandelic acid)  
(HO—, HO—C<sub>6</sub>H<sub>3</sub>) (H) C (OH) COOH

## (3) Polyhydroxy-Carboxylic Acids

1. 2,3-Dihydroxypropanoic acid (Glyceric acid)  
(HOCH<sub>2</sub>) (H) C (OH) COOH
2. 2,3,4-Trihydroxybutanoic acid (Isomers; erythronic acid, threonic acid)  
(HOCH<sub>2</sub> HOCH) (H) C (OH) COOH

## 5

3. 2,3,4,5-Tetrahydroxypentanoic acid (Isomers; ribonic acid, arabinic acid, xylonic acid, lyxonic acid)  
(HOCH<sub>2</sub> HOCH HOCH) (H) C (OH) COOH
4. 2,3,4,5,6-Pentahydroxyhexanoic acid (Isomers; allonic acid, altronic acid, gluconic acid, mannoic acid, gulonic acid, idonic acid, galactonic acid, talonic acid)  
(HOCH<sub>2</sub> HOCH HOCH HOCH) (H) C (OH) COOH
5. 2,3,4,5,6,7-Hexahydroxyheptanoic acid (Isomers; glucoheptonic acid, galactoheptonic acid etc.)  
(HOCH<sub>2</sub> HOCH HOCH HOCH HOCH) (H) C (OH) COOH

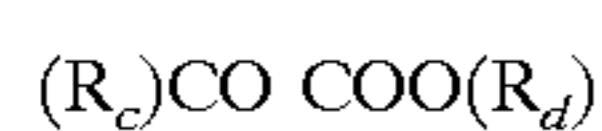
## (4) Hydroxy-Polycarboxylic Acids

1. 2-Hydroxypropane-1,3-dioic acid (Tartronic acid)  
(HOOC) (H) C (OH) COOH
2. 2-Hydroxybutane-1,4-dioic acid (Malic acid)  
(HOOC CH<sub>2</sub>) (H) C (OH) COOH
3. 2,3-Dihydroxybutane-1,4-dioic acid (Tartaric acid)  
(HOOC HOCH) (H) C (OH) COOH
4. 2-Hydroxy-2-carboxypentane-1,5-dioic acid (Citric acid)  
(HOOC CH<sub>2</sub>)<sub>2</sub> C (OH) COOH
- 2,3,4,5-Tetrahydroxyhexane-1,6-dioic acid (Isomers; saccharic acid, mucic acid etc.)  
HOOC (CHOH)<sub>4</sub> COOH

The 2-hydroxycarboxylic acids may be present in forms other than the acid, such as, for example, salts or lactones. Typical lactone forms which may be used in accordance with this invention include, for example, gluconolactone, galactonolactone, glucuronolactone, galacturonolactone, gulonolactone, ribonolactone, saccharic acid lactone, pantoyllactone, glucoheptonolactone, mannonolactone, and galactoheptonolactone.

## Group 2

The second group, which comprises compounds related to the 2-hydroxycarboxylic acids, includes organic carboxylic acids in which one keto group is attached to position 2 carbon atom of the acid. The generic structure of such 2-ketoacids may be represented as follows:



wherein R<sub>c</sub> and R<sub>d</sub> can be the same or different and are each selected from H, alkyl, aralkyl or aryl group of saturated or unsaturated, isomeric or non-isomeric, straight or branched chain or cyclic form, having 1 to 29 carbon atoms, and in addition RC may carry F, Cl, Br, I, OH, CHO, COOH and alkoxy group having 1 to 9 carbon atoms. The alpha ketoacids may be present as a free acid or an ester form, or in a salt form with an organic base or an inorganic alkali. The typical alkyl, aralkyl and aryl groups for R<sub>c</sub> and R<sub>d</sub> include methyl, ethyl, propyl, 2-propyl, butyl, pentyl, hexyl, octyl, dodecyl, hexadecyl, benzyl and phenyl.

In contrast to 2-hydroxycarboxylic acids of the first group compounds, the ester form of 2-ketocarboxylic acids has been found to be therapeutically effective for signs and symptoms of cutaneous aging including intrinsic and extrinsic aging. For example, while methyl 2-hydroxypropanoate and ethyl 2-hydroxypropanoate have minimal effects, methyl 2-ketopropanoate and ethyl 2-ketopropanoate are therapeutically very effective. The real mechanism for such difference is not known. We have speculated that the ester form of the 2-ketocarboxylic acid is chemically and/or biochemically very reactive, and a free 2-ketocarboxylic acid may be released in the skin after penetration through the

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stratum corneum of the skin. The representative 2-ketocarboxylic acids and their esters of the second group are listed below:

1. 2-Ketoethanoic acid (Glyoxylic acid)  
(H) CO COOH
2. Methyl 2-ketoethanoate  
(H) CO COOCH<sub>3</sub>
3. 2-Ketopropanoic acid (Pyruvic acid)  
CH<sub>3</sub> CO COOH
4. Methyl 2-ketopropanoate (Methyl pyruvate)  
CH<sub>3</sub> CO COOCH<sub>3</sub>
5. Ethyl 2-ketopropanoate (Ethyl pyruvate)  
CH<sub>3</sub> CO COOC<sub>2</sub>H<sub>5</sub>
6. Propyl 2-ketopropanoate (Propyl pyruvate)  
CH<sub>3</sub> CO COOC<sub>3</sub>H<sub>7</sub>
7. 2-Phenyl-2-ketoethanoic acid (Benzoylformic acid)  
C<sub>6</sub>H<sub>5</sub> CO COOH
8. Methyl 2-phenyl-2 ketoethanoate (Methyl benzoylformate)  
C<sub>6</sub>H<sub>5</sub> CO COOCH<sub>3</sub>
9. Ethyl 2-phenyl-2-ketoethanoate (Ethyl benzoylformate)  
C<sub>6</sub>H<sub>5</sub> CO COOC<sub>2</sub>H<sub>5</sub>
10. 3-Phenyl-2-ketopropanoic acid (Phenylpyruvic acid)  
C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub> CO COOH
11. Methyl 3-phenyl-2-ketopropanoate (Methyl phenylpyruvate)  
C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub> CO COOCH<sub>3</sub>
12. Ethyl 3-phenyl-2-ketopropanoate (Ethyl phenylpyruvate)  
C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub> CO COOC<sub>2</sub>H<sub>5</sub>
13. 2-ketobutanoic acid  
C<sub>2</sub>H<sub>5</sub> CO COOH
14. 2-Ketopentanoic acid  
C<sub>3</sub>H<sub>7</sub> CO COOH
15. 2-Ketohexanoic acid  
C<sub>4</sub>H<sub>9</sub> CO COOH
16. 2-Ketoheptanoic acid  
C<sub>5</sub>H<sub>11</sub> CO COOH
17. 2-Ketooctanoic acid  
C<sub>6</sub>H<sub>13</sub> CO COOH
18. 2-Ketododecanoic acid  
C<sub>10</sub>H<sub>21</sub> CO COOH
19. Methyl 2-ketooctanoate  
C<sub>6</sub>H<sub>14</sub> CO COOCH<sub>3</sub>

## Group 3

The third group, which also comprises related compounds, includes, among others, hydroxycarboxylic acids where the hydroxy is at a position other than position 2, and cyclic hydroxycarboxylic acids which are useful for topical application to improve signs of aging skin and the cutaneous appendages. The members of this group, which are more conveniently identified by name than by generic structures, include salicylic and other beta-hydroxy carboxylic acids as well as, ascorbic acid, quinic acid, isocitric acid, tropic acid (2-phenyl 3-hydroxypropanoic acid), trethocanic acid, 3-chlorolactic acid, citramalic acid, agaricic acid, alcuritic acid, pantoic acid, lactobionic acid and hexulosonic acid.

The acerola cherry is not, in fact, a true cherry but has come to include the cherry-like berries that are produced by any of several shrubs of the Malpighia family. These cherry-like berries are also known by other names depending on

where they are produced, for instance, West Indian cherry, Barbados cherry, Surinam cherry, and Cereza. The term "acerola cherry" as used in the specification and appended claims is intended to be generic for all of these different berries of the Malpighia family.

The acerola cherry fermentate used in the present invention contains only a minor amount of organic acids, particularly carboxylic acids, which includes saturated and unsaturated carboxylic and dicarboxylic acids, hydroxymonocarboxylic acids, hydroxydicarboxylic acids, and hydroxytricarboxylic acids. In particular, any organic acid or carboxylic acid present in the acerola cherry fermentate is present in an amount no greater than about 5% by weight, preferably no greater than about 3%, and more preferably no greater than about 2% of the acerola cherry fermentate.

The acerola cherry fermentate can be made in any suitable manner to achieve an extract that contains only a minor amount of organic acids, preferably less than about 5% of organic acids. The raw acerola cherry used to make the fermentate may be brown, green, yellow, red or a mixture of two or more, depending upon the availability.

Preferably, the acerola cherry fermentate is obtained from Collaborative Laboratories (NY) and it is believed that the process for making the Acerola cherry fermentate useful in the composition of the present invention is as follows. A cherry extract is prepared by washing the bulk cherries, pitting them and then reducing them to a puree, which is subjected to shearing and extraction with water whereby a filtrate is produced. Thereafter, the filtrate is fermented using a bacteria, preferably a bacteria from the lactobacillus family, to produce a fermentate that is separated from the bulk filtrate. The separated fermentate is the acerola cherry fermentate useful in the present invention.

In the composition according to the present invention, the amount of acerola cherry fermentate to be used can not be absolutely specified because it varies according to the form of the preparation. It is, however, generally used in an amount from about 0.01% to about 50%, more generally from about 0.1% to about 10%. Preferably the acerola cherry fermentate is used in an amount from about 0.5% to about 8%, more preferably from about 1% to about 5% based on the whole weight of the composition.

Another aspect of the present invention includes a method of increasing the rate of skin exfoliation or desquamation comprising topically applying a composition containing at least one organic acid and an enhancing effective amount of acerola cherry fermentate. In this aspect, the method includes topically applying to the skin a composition comprising an organic acid and acerola cherry fermentate, in an amount and for a period of time sufficient to increase the rate of natural skin desquamation.

Surprisingly, the advantageous results achieved by the incorporation of the acerola cherry fermentate are realized even though the acerola cherry fermentate contains only a minor amount of organic acids.

To prepare a therapeutic composition in solution form, at least one of the aforementioned organic acids and acerola cherry fermentate are incorporated into pharmaceutically acceptable vehicles. Desirably, the organic acid is selected from the group consisting of lactic acid, malic acid, citric acid, glycolic acid and mixtures thereof.

The concentration of organic acid may range from about 0.01 to about 99 percent by weight of the total composition. Preferably, the concentration of organic acid ranges from about 0.1% to about 70%, more preferably from about 1% to about 15%, and desirably from about 1% to about 10%.

The concentration of the acerola cherry fermentate ranges from about 0.01 to about 99 percent by weight of the total composition. Preferably, the concentration of acerola cherry fermentate ranges from about 0.05% to about 30%, more preferably from about 0.1% to about 10%.

Desirably, the ratio of organic acid to acerola cherry fermentate ranges from about 1:1 to about 100:1. It is believed that when the ratio of the organic acid to the acerola cherry fermentate is within this range that irritation of acid is reduced and cell renewal rate is incremental. Within this ratio, it is desired to have a composition with a pH between about 3.0 and about 5.0, preferably between about 3.5 and about 4.5, more preferably, between about 3.8 and about 4.2.

Therapeutic compositions of the present invention may be formulated as a solution, gel, lotion, cream ointment, or other pharmaceutically acceptable form. The compositions of the present invention may also contain various known and conventional cosmetic ingredients so long as they do not detrimentally affect the desired enhancement of skin desquamation. For example, cosmetic ingredients such as alcohols, fats and oils, surfactants, fatty acids, silicones, humectants, moisturizers, viscosity modifiers, emulsifiers, stabilizers, coloring agents, and perfumes or fragrances may be included.

Examples of suitable fatty acids include those chosen from linoleic acid,  $\gamma$ -linolenic acid, homo- $\gamma$ -linolenic acid, columbinic acid, eicosa-(n-6,9,13)-trienoic acid, arachidonic acid,  $\alpha$ -linolenic acid, timnodonic acid, hexaenoic acid and mixtures thereof.

Non-essential fatty acids can also be employed in addition to or in place of essential fatty acids, examples of which are chosen from myristic, palmitic, stearic and isostearic acids, and mixtures thereof.

The composition according to the invention also comprises a cosmetically acceptable aqueous or non-aqueous vehicle to act as a diluant, dispersant or carrier to facilitate distribution when the composition is applied to the skin, hair and/or nails.

Vehicles other than water can include liquid or solid emollients, solvents, humectants, thickeners and powders. Examples of each of these types of vehicle, which can be used single or as mixtures of one or more vehicles, are as follows:

Emollients, such as stearyl alcohol, glyceryl monoricinoleate, glyceryl monostearate, mink oil, cetyl alcohol, isopropyl isostearate, stearic acid, isobutyl palmitate, isocetyl stearate, oleyl alcohol, isopropyl laurate, hexyl laurate, decyl oleate, octadecan-2-ol, isocetyl alcohol, eiconsanyl alcohol, behenyl alcohol, cetyl palmitate, volatile or non-volatile silicone oils such as dimethylpolysiloxane, di-n-butyl sebacate, isopropyl myristate, isopropyl palmitate, isopropyl stearate, butyl stearate, poethylene glycol, triethylene glycol, lanolin, cocoa butter, corn oil, cotton seed oil, tallow, lard, olive oil, palm kernel oil, rapeseed oil, safflower seed oil, evening primrose oil, soybean oil, sunflower seed oil, passion flower oil, avocado oil, olive oil, sesame seed oil, coconut oil, arachis oil, castor oil, acetylated lanolin alcohols, petroleum jelly, mineral oil, butyl myristate, isostearic acid, palmitic acid, isopropyl linoleate, lauryl lactate, myristyl lactate, decyl oleate, myristyl myristate;

Propellants, such as air, propane, butane, isobutane, dimethyl ether, carbon dioxide, nitrous oxide;

Solvents such as ethyl alcohol, methylene chloride, isopropanol, acetone, squalane, squalene, ethylene glycol monethyl ether, diethylene glycol monobutyl ether, diethyl-

ene glycol monoethyl ether, polyethylene glycol, dimethyl sulphoxide, dimethyl formamide, butylene glycol, tetrahydrofuran;

Powders such as chalk, talc, fullers earth, kaolin, starch, gums, colloidal silica sodium polyacrylate, tetra alkyl and/or trialkyl aryl ammonium smectites, chemically modified magnesium aluminum silicate, organically modified montmorillonite clay, hydrated aluminum silicate, fumed silica, carboxyvinyl polymer, sodium carboxymethyl cellulose, ethylene glycol monostearate.

The cosmetically acceptable vehicle will usually form from 10 to 99.9%, preferably from 50 to 99% by weight of the emulsion, and can, in the absence of other cosmetic adjuncts, form the balance of the composition.

Although the composition according to the invention can be aqueous or non-aqueous, a particularly convenient form is an emulsion, in which case an oil or oily material will normally be present, together with an emulsifier to provide a water-in-oil emulsion, an oil-in-water emulsion, or a complex emulsion, depending largely on the average hydrophilic-lipophilic balance (HLB) of the emulsifier employed.

The composition can optionally comprise one or more oils or other materials having the properties of an oil. Examples of suitable oils include mineral oil and vegetable oils, and oil materials, such as those already proposed herein as emollients. Other oils or oily materials include silicone oils, both volatile and non-volatile, such as polydimethyl siloxanes. The oil or oily material, when present for the purposes for forming an emulsion, will normally form up to 90%, preferably from 10 to 80% by volume of the composition.

The composition can also optionally comprise one or more emulsifiers the choice of which will normally determine whether a water-in-oil or and oil-in-water emulsion is formed. When a water-in-oil emulsion is required, the chosen emulsifier or emulsifiers should normally have an average HLB value of from 1 to 6. When an oil-in-water emulsion is required, a chosen emulsifier or emulsifiers should have an average HLB value of >6.

Examples of suitable emulsifiers are set below in Table 1 in which the chemical name of the emulsifiers is given together with an example of a trade name as commercially available, and the average HLB value.

TABLE 1

Chemical Name of Emulsifier	Trade Name	HLB Value
Sorbitan trioleate	Arlacel 85	1.8
Sorbitan tristearate	Span 65	2.1
Glycerol monooleate	Aldo MD	2.7
Glycerol monostearate	Atmul 84S	2.8
Glycerol monolaurate	Aldo MC	3.3
Sorbitan sesquioleate	Arlacel 83	3.7
Sorbitan monooleate	Arlacel 80	4.3
Sorbitan monostearate	Arlacel 60	4.7
Polyoxyethylene (2) stearyl ether	Brij 72	4.9
Polyoxyethylene sorbitol beeswax derivative	G-1702	5
PEG 200 dilaurate	Emerest 2622	6.3
Sorbitan monopalmitate	Arlacel 40	6.7
Polyoxyethylene (3.5) nonyl phenol	Emulgen 903	7.8
PEG 200 monostearate	Tegester PEG 200 MS	8.5
Sorbitan monolaurate	Arlacel 200	8.6
	400-DO	8.8

TABLE 1-continued

	Chemical Name of Emulsifier	Trade Name	HLB Value
5	Polyoxyethylene (5) monostearate	Ethofat 60-16	9.0
	Polyoxyethylene (4) sorbitan monostearate	Tween 61	9.6
	Polyoxyethylene (4) lauryl ether	Brij 30	9.7
10	Polyoxyethylene (5) sorbitan monooleate	Tween 81	10.0
	PEG 300 monooleate	Neutronyx 834	10.4
	Polyoxyethylene (20) sorbitan tristearate	Tween 65	10.5
15	Polyoxyethylene (20) sorbitan trioleate	Tween 85	11.0
	Polyoxyethylene (8) monostearate	Myrj 45	11.1
	PEG 400 monooleate	Emerest 2646	11.7
	PEG 400 monostearate	Tegester PEG 400	11.9
20	Polyoxyethylene 10 monooleate	Ethofat 0/20	12.2
	Polyoxyethylene (10) stearyl ether	Brij 76	12.4
	Polyoxyethylene (10) cetyl ether	Brij 56	12.9
25	Polyoxyethylene (9.3) octyl phenol	Triton X-100	13.0
	Polyoxyethylene (4) sorbitan monolaurate	Tween 21	13.3
	PEG 600 monooleate	Emerest 2660	13.7
	PEG 1000 dilaurate	Kessco	13.9
	Polyoxyethylene sorbitol lanolin derivative	G-1441	14.0
30	Polyoxyethylene (12) lauryl ether	Ethospense LA-12	14.4
	PEG 1500 dioleate	Pegospense 1500	14.6
	Polyoxyethylene (14) laurate	Arosurf HFL-714	14.8
35	Polyoxyethylene (20) sorbitan monostearate	Tween	14.9
	Polyoxyethylene 20 sorbitan monooleate	Tween 80	15.0
	Polyoxyethylene (20) stearyl ether	Brij 78	15.3
40	Polyoxyethylene (20) sorbitan monopalmitate	Tween 40	15.6
	Polyoxyethylene (20) cetyl ether	Brij 58	15.7
	Polyoxyethylene (25) oxypropylene monostearate	G-2162	16.0
45	Polyoxyethylene (20) sorbitol monolaurate	Tween 20	16.7
	Polyoxyethylene (23) lauryl ether	Brij 35	16.9
	Polyoxyethylene (50) monostearate	Myrj 53	17.9
50	PEG 4000 monostearate	Pegospense 4000 MS	18.7

The foregoing list of emulsifiers is not intended to be limiting and merely exemplifies selected emulsifiers which are suitable for use in accordance with the invention. It is to be understood that two or more emulsifiers can be employed if desired.

The amount of emulsifier or mixtures thereof, to be incorporated in the composition of the invention, when appropriate is from 1 to 50%, preferably from 2 to 20% and most preferably from 2 to 10% by weight of the composition.

Although the composition of the invention can be anhydrous, it can also comprise water, usually up to 98%, preferably from 5 to 80% by volume.



The composition of the invention can also optionally comprise a high molecular weight silicone surfactant which can also act as an emulsifier, in place of or in addition to the optional emulsifiers already mentioned. One example of a suitable silicone surfactant is a high molecular weight polymer of dimethyl polysiloxane with polyoxyethylene and/or polyoxypropylene side chains having a molecular weight of from 10,000 to 50,000. The dimethyl polysiloxane polymer is may be provided as a dispersion in a volatile siloxane, the dispersion comprising, for example, from 1 to 20% by volume of the polymer and from 80 to 99% by volume of the volatile siloxane. Ideally, the dispersion consists of a 10% by volume of the polymer dispersed in the volatile siloxane. Examples of the volatile siloxanes in which the polysiloxane polymer can be dispersed include polydimethyl siloxane (pentamer and/or hexamer).

A preferred silicone surfactant is cyclomethicone and dimethicone copolyol, such as DC 3225C Formulation Aid available from DOW CORNING. Another is laurylmethicone copolyol, such as DC Q2-5200, also available from Dow Corning.

The amount of silicone surfactant, when present in the composition will normally be from 0.1% to 25%, preferably from 0.5 to 15% by weight of the emulsion.

Examples of other conventional adjuncts which can optionally be employed include preservatives, such as parahydroxy benzoate esters; antioxidants, such as  $\alpha$ -tocopherol, humectants, such as glycerol, sorbitol, 2-pyrrolidone-5-carboxylate, dibutylphthalate, gelatin, polyethylene glycol, preferably PEG 200-600; buffers, such as lactic acid together with a base such as triethanolamine or sodium hydroxide; surfactants, such as glycerol ethers; waxes, such as beeswax, ozokerite wax, paraffin wax, plant extracts, such as aloe Vera, cornflower, witch hazel, elderflower, cucumber; thickeners; activity enhancers; colorants; perfumes; and sunscreen materials such as ultrafine titanium dioxide and organic sunscreens such as p-aminobenzoic acid and esters thereof, ethylhexyl p-methoxycinnamate, 2-ethoxyethyl p-methoxycinnamate and butyl methoxydibenzoylmethane; and skin benefit agents, such as retinoic acid, retinol, retinol esters; anti-inflammatory agents, such as salicylic acid; skin whiteners, such as arbutin and mixtures thereof.

In accordance with one aspect of the present invention, the rate of natural skin desquamation may be increased by topical application to the skin of the above composition. In this regard, the present invention encompasses a method of enhancing the rate of natural skin desquamation comprising topically applying to the skin a composition comprising an organic acid and acerola cherry fermentate in an amount and for a period of time sufficient to increase the rate of natural skin desquamation. Preferably, the composition is as described above.

Generally, the topical application is on at least a daily basis and may be applied for any suitable period of time. Within a few days, a user may notice improvement in skin texture and smoothness.

The present invention also includes a method of enhancing a composition used for skin desquamation and including an organic acid wherein the method includes incorporating an enhancing effective amount of acerola cherry fermentate.

The following are illustrative examples of formulations and compositions according to this invention. Although the examples use only selected compounds and formulations, it should be understood that the following examples are illustrative and not limited. Thus, any of the aforementioned

organic acids and related compounds may be substituted according to the teachings of this invention in the following examples.

Table 2 sets forth a preferred embodiment of a lotion according to the present invention.

TABLE 2

INGREDIENT	AMOUNT (wt %)
Lactic Acid (88% active)	4.50
Citric, Malic, and Lactic acid mixture (30-40% active)	3.00
Acerola Cherry Fermentate (1.8-3% active acid)	3.00
Glyceryl monostearate PEG 100 Stearate	3.00
Sodium Hydroxide	2.30
Glycerin	2.00
Butylene Glycol	2.00
Dimethicone	2.00
Stearic Acid	2.00
Phenonip	0.75
Sorbitan Stearate	0.50
Magnesium Aluminum Silicate	0.40
Cetyl Alcohol	0.25
Xanthan Gum	0.20
Methylparaben	0.15
Water and adjuncts	qs to 100.00
TOTAL	100.00

Adjuncts include but are not limited to preservatives such as methyl paraben, phenonip, gums such as magnesium aluminum silicate, hydroxyethyl cellulose, and xanthan gum, humectants such as panthenol, glycerin and butylene glycol, waxes such as sorbitan stearate and glyceryl monostearate and PEG 100 stearate, stearic acid, cetyl alcohol, skin conditioning agents such as alkyl benzoates, dimethicone, lipids, hyaluronic acid and salts thereof, green tea, ginko biloba, polyglyceryl methacrylate, propylene glycol.

Table 3 presents a gel-type formula falling within the scope of the present invention with the amounts provided being expressed as weight percent.

TABLE 3

INGREDIENT	AMOUNT (wt %)
Lactic Acid (88% active acid)	2.25
Citric, Malic, and Lactic acid mixture (30-40% active)	3.00
Acerola Cherry Fermentate (1.8-3% active acid)	3.00
PEG-20	5.00
Glycerin	4.00
Polyglyceryl methacrylate, Propylene Glycol	4.00
Butylene Glycol	3.00
Sodium Hydroxide	1.40
Hydroxyethyl cellulose	0.40
Xanthan gum	0.40
Saccharide isomerate	0.30
Water and adjuncts	qs to 100.00
TOTAL	100.00

In order to determine whether compositions containing organic acids and acerola cherry fermentate were therapeutically effective in enhancing the natural rate of skin desquamation the following tests were conducted. The skin cell renewal, irritation level and therapeutic index were measured according to the procedure described in *Soap/*

*Cosmetics/Chemical Specialties* for September 1993 at pp.55-59.

TABLE 4

Formula	AHA* %	Acerola Fermentate %	% Cell Renewel	Irritation Level	Therapeutic Index
A	3.0	0	12.2	11.4	10.7
B	3.0	3.0	19.8	15.6	11.5
C	3.0	3.0	21.4	16.8	12.7
D	5.0	3.0	19.8	14.2	14.0
E	5.0	3.0	18.9	14.1	13.4
F	5.0	3.0	22.6	13.1	17.3

\*AHA refers to the total amount of active hydroxycarboxylic acid selected from glycolic acid, malic acid, citric acid, lactic acid and mixtures thereof.

Formulas A-E were made according to the formula set forth in Table 2 with the amounts of water and alpha-hydroxy acid being varied so that the alpha-hydroxy acid was present in the amounts shown in Formulas A-E, above. Formula F was made according to the formula set forth in Table 3 with the amount of water and alpha-hydroxy acid varied to the level shown for Formula F. The results show that the addition of the acerola cherry fermentate surprisingly and unexpectedly significantly increased cell renewal rate while only slightly increasing irritation.

It should be understood that a wide range of changes and modifications can be made to the compositions and methods of this invention. It is therefore intended that the foregoing description illustrates rather than limits this invention, and that it is the following claims, including all equivalents, which define this invention.

What is claimed:

1. A method of enhancing the rate of mammalian skin desquamation comprising topically applying to the skin a composition comprising:

a first organic acid selected from the group consisting of glycolic, malic, citric and salts thereof and mixtures thereof, and

acerola cherry fermentate, the acerola cherry fermentate containing a minor amount of a second organic acid.

2. The method of claim 1 wherein the acerola cherry fermentate contains less than about 5% of the second organic acid based on the weight of the acerola cherry fermentate.

3. The method of claim 2 wherein the second organic acid is selected from the group consisting of glycolic, malic, citric, and lactic acid, salts thereof and mixtures thereof.

4. The method of claim 1, wherein the composition is formulated as a solution, gel, lotion, cream or ointment.

5. The method of claim 1 wherein the composition is topically applied in an amount and for a period of time sufficient to enhance the rate the skin desquamation.

6. The method of claim 5 wherein the topical application is on at least a daily basis.

7. A method of increasing the rate of mammalian skin desquamation comprising the step of topically applying to the skin a composition comprising a first organic acid selected from the group consisting of glycolic, malic, citric and salts thereof and mixtures thereof and acerola cherry fermentate containing a second organic acid wherein the acerola cherry fermentate enhances the rate of skin desquamation achieved by the first organic acid.

8. The method of claim 7 wherein the acerola cherry fermentate causes only slight additional skin irritation when the composition is applied to the skin.

9. The method of claim 7 wherein the acerola cherry fermentate comprises from about 1% to about 5% by weight of the composition based on the whole weight of the composition.

10. The method of claim 7 wherein the acerola cherry fermentate contains no more than 5% by weight of the second organic acid based on the weight of the acerola cherry fermentate.

11. A method of increasing human skin exfoliation rate of mammalian skin achieved by a first organic acid selected from the group consisting of glycolic, malic, citric and salts thereof and mixtures thereof comprising the step of adding acerola cherry fermentate, wherein the acerola cherry fermentate contains a second organic acid in an amount no greater than 5% by weight of the acerola cherry fermentate.

12. The method of claim 11 wherein the acerola cherry fermentate causes only slight additional skin irritation when the composition is applied to the skin.

13. The method of claim 11 wherein the acerola cherry fermentate contains no more than 2% by weight of the second organic acid based on the weight of the acerola cherry fermentate.

\* \* \* \* \*

UNITED STATES PATENT AND TRADEMARK OFFICE  
**CERTIFICATE OF CORRECTION**

PATENT NO. : 6,074,647  
DATED : June 13, 2000  
INVENTOR(S) : A. C. Zimmerman et al.

Page 1 of 1

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Title page, Page 3,  
Column 2,

After line 17, insert the following reference:

-- Photocopy of front and back of product container, Vaseline® Brand Intensive Care®  
Lotion. --.

Signed and Sealed this

Ninth Day of October, 2001

*Attest:*

*Nicholas P. Godici*

*Attesting Officer*

NICHOLAS P. GODICI  
*Acting Director of the United States Patent and Trademark Office*